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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/873,637	06/04/2001	Jeffrey Ross	960296.98164	5237

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QUARLES & BRADY LLP  
411 E. WISCONSIN AVENUE, SUITE 2040  
MILWAUKEE, WI 53202-4497

EXAMINER

YU, MISOOK

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 01/13/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/873,637	ROSS, JEFFREY
	Examiner	Art Unit
	MISOOK YU, Ph.D.	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 30 October 2002.

2a) This action is **FINAL**.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-27 is/are pending in the application.

4a) Of the above claim(s) 1-15 and 17-20 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 16 and 21-27 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,6.

4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_.

## DETAILED ACTION

### ***Election/Restrictions***

Claims 1-15, 17-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

Claims 1-27 are pending and claims 16, and 21-27 are examined on merits.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16, and 21-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 16, and 21-27 are confusing, therefore indefinite because it is not clear what is being claimed by instant claims for patent protection. The preamble of claim 16 says that the instant claims are drawn to a method of determining the presence or absence of an autoantibody to CRD-BP protein in serum sample of a patient but claim 23 appears to be saying that the instant invention is drawn to method of diagnosing cancer by detecting the autoantibody. The claims could be interpreted as drawn to cancer screening method by detecting the autoantibody. The claims, as written, could be also interpreted as a research proposal of assessing if the autoantibody exists in serum sample of a patient and if it does, then figuring out if it could be used as a marker for cancer. Note the paragraph bridging pages 19 and 20 of the instant specification. For the purpose of this office action, the examiner will assume that the instant claims are drawn to cancer screening method using an autoantibody to CRD-BP as a biomarker since a method of assessing whether an autoantibody to CRD-BP is present in serum of patient and whether the autoantibody could be used as a biomarker (the second

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interpretation above) are just an invitation for further research, i.e., not a substantial, specific or credible utility. However, this treatment does not relieve applicant the burden of responding this rejection.

Claims 22 and 23 recite "antibody" but it is not clear what the metes and bounds are for the limitation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, and 21-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to **use** the invention. Claims 16, and 21-27 are interpreted as a method of cancer diagnosis by detecting an autoantibody to CRD-BP. The specification at the paragraph bridging pages 19 and 20 says that it would be very nice if an autoantibody to CRD-BP exists in serum of cancer because it might be used as a biomarker for cancer detection.

One cannot extrapolate the teachings of the specification to the claimed invention because cancer diagnosis is not trivial matter (unpredictable) and the specification provides neither guidance on nor exemplification of how to use the invention for the assessment of cancer risk. It is not clear whether presence of an autoantibody to CRD-BP is involved in development of cancer <sup>in</sup> vivo. Jalbout et al (2002, Int. J. Cancer, vol., 101, pages 146-150) teach that it takes undue experimentation involving a large quantity of clinical samples along with aged matched control group to determine if autoantibodies to a human protein could be used as a biomarker for a specific cancer. Note Materials and Methods section, Table 1-III and Figures 1 and 2. Further, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker to successful clinical application. Although the reference is drawn to biomarkers for early lung cancer detection, the basic principles taught are clearly

applicable to instant invention. Tockman et al teach that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of tumorigenicity have clear biological plausibility as markers of preclinical cancer and if validated can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and link those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2).

The specification provides insufficient guidance, and provides no working examples of correlating in vivo cancer to autoantibodies to CRD-BP would provide guidance to one skilled in the art to use the claimed invention without undue experimentation. Considering lack of examples and the limited teachings of the specification, and unpredictability in the art, it is concluded that undue experimentation would be required to practice the claimed invention.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Misook Yu  
January 9, 2003



MARY E. MOSHER  
PRIMARY EXAMINER  
GROUP 1800